REMARKS

This application is a national phase filing under 35 U.S.C. §371 of International Application No. PCT/JP2004/019226 filed May 30, 2007. The PCT application, with an International Filing date of December 22, 2004, claims priority to Japanese Patent Application Serial No. 2003-425706, filed December 22, 2003. At the time the application was filed, claims 1-6 were pending and claims 1, 4 and 5 were amended in a Preliminary Amendment filed with the application. In their March 12, 2010 Response, Applicants amended claims 1 and 6, canceled claims 2 and 4, and added new claims 7-10. On December 3, 2010 Applicants filed a Request for Continued Examination (RCE) and a Response to a Final Office Action, wherein Applicants amended claims 1 and 6-9. Currently, Applicants amend claim 3 and cancel claim 9. Claims 1, 3, 5-8, and 10 are currently pending in the application.

The Examiner's rejections are addressed below. Reconsideration of the application and allowance of all claims pending herein are respectfully requested in view of the following remarks.

I. OBJECTIONS & CLAIM REJECTIONS UNDER 35 U.S.C. § 112

The Office Action rejects claims 1, 3, 5, and 7-10 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Office Action states that claim 1 is indefinite in reciting "lower level" because the term "lower" is a subjective term lacking a comparative basis for defining its metes and bounds. Applicants respectfully disagree and urge that the term "lower is definite because a person having ordinary skill in the art would readily understand the term when it is read in light of Applicants' disclosure.

"The test for definiteness under 35 U.S.C. 112, second paragraph, is whether 'those skilled in the art would understand what is claimed when the claim is read in light of the specification.'" (MPEP § 2173.02 (citing *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806

F.2d 1565, 1576 (Fed. Cir. 1986)). Applicants respectfully submit that, notwithstanding the recitation "lower", a skilled artisan would readily understand what Applicants are claiming. This is especially true in light of the specification. The Action states that the term lacks a comparative basis for defining its metes and bounds, but the claims recite that the vWF-cp is compared to that which would be present in a normal person, which is an appropriate comparative basis. The term does *not* render the claim "such that a person of ordinary skill in the art could not interpret the metes and bounds of the claim so as to understand how to avoid infringement," and therefore the language satisfies the requirements of §112, second paragraph, and an indefiniteness rejection is inappropriate (MPEP § 2173.02). Reconsideration is respectfully requested.

The Office Action states that claim 3 is indefinite in lacking antecedent basis in reciting "the degree of thrombophilia." Claim 1, from which claim 3 depends, previously recited "degree of thrombophilia", but was amended in Applicants' December 3, 2010 Response to recite "severity of thrombophilia." Accordingly, currently, Applicants amend claim 3 such that it recites "~~degree~~ severity of thrombophilia", which takes proper antecedent basis from claim 1.

The Office Action states that claim 7 is objected to in failing to further limit the claimed invention in reciting, "the bodily fluid is blood plasma." Claim 7 is an independent claim which recites that the bodily fluid is "selected from the group consisting of **whole blood, blood plasma, and serum**". It appears that this objection is actually directed to claim 8, which recites "[t]he method of claim 7, where the bodily fluid is **blood plasma**." Applicants respectfully submit that claim 8 properly further narrows the invention as recited in claim 7 insofar as claim 8 specifies that the bodily fluid is blood plasma, as opposed to whole blood or serum.

The Office Action also objects to claim 8 for failing to further limit the claimed invention in reciting "diseases selected from the group consisting of pulmonary embolism, cerebral infarction, veno-occlusive disease, and deep vein thrombosis." It appears that this objection is actually directed to claim 9, which recites the referenced language. Claim 9 has been canceled.

II. CLAIM REJECTIONS UNDER 35 U.S.C. § 102

A. Rejection of Claims 1, 3, and 5-10 as Anticipated by Scheiflinger

The Office Action rejects claims 1, 3, and 5-10 under 35 U.S.C. § 102(a) as being anticipated by Scheiflinger *et al.* (U.S. 2004/0214346 A1) (hereinafter referred to as "Scheiflinger"). Claim 9 has been canceled. Claims 1, 6, and 7 are independent, and the remaining rejected claims depend from, and add limitations to claim 1 or claim 7.

In order to anticipate a claim, a reference must set forth each and every element of the claim (*see* MPEP § 2131). Applicants respectfully submit that claims 1, 3, 5-8, and 10 are not anticipated by Scheiflinger because the reference does not contain all of the elements of Applicants' claims. *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379 (Fed. Cir. 1986); *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569 (Fed. Cir. 1984).

Scheiflinger explains that its "invention relates to a kit to be used in an assay system for determination of **an anti-von Willebrand Factor-cleaving protease** (ADAMTS13) **antibody** ("anti-vWF-cp antibody") in a sample suspected to comprise an anti-vWF-cp antibody." Scheiflinger, p. 1, para. [001]. Scheiflinger explains that prior art assays *only* allowed for detection of vWF-cp inhibitory antibodies that impair the catalytic activity of vWF-cp. *See id.*, p. 1, para. [0007]. Scheiflinger's invention, on the other hand, allows for detection of vWF-cp inhibitory antibodies that impair vWF-cp functions other than the enzyme's catalytic activity. *See id.*, para. [0008]. Scheiflinger explains that he utilized an enzyme-linked immunosorbent assay (ELISA), wherein immobilized vWF-cp and/or vWF-cp fragment(s) are placed in wells on the solid phase. Scheiflinger determined the presence of anti-vWF-cp antibodies by adding a patient's diluted plasma samples to the recombinant vWF-cp-containing wells. In this assay,"[i]nhibitory antibodies are bound on the surface of the immobilized vWF-cp and unbound antibodies are washed away", then "[d]etection of human antibodies is performed..." and a substrate is added to "result[] in a yellow color, whereby the color intensity reflects the amount of bound antibody (antibody/vWF-cp). The color intensity is measured ... and the amount of antibody within the plasma sample is calculated...", so that "human anti-vWF-cp antibodies in a patient[] can be clearly detected" *See* Scheiflinger, pp. 4-5, para. [0050]. Scheiflinger states

that with this assay system, "the complete spectrum of anti-vWF-cp antibodies can be captured and anti-vWF-cp antibodies having specific binding activity within a region/domain of vWF-cp are identified." *Id.*, p. 3., para. [0028]. Scheiflinger explains that his system "allows one to discriminate between anti-vWF-cp antibodies having different specificities and based on impairment of different biological functions of vWF-cp", which allowed him to determine vWF-cp inhibitory antibodies that were not detected in prior art systems. *Id.*, p. 1, para. [0010].

As explained above, Scheiflinger is directed to the discovery of nonneutralizing antibodies. The **antibodies** were determined by contacting a patient's plasma samples containing the antibodies with Scheiflinger's enzyme-linked immunosorbent assay, which included recombinant vWF-cp-containing wells, then identifying and quantifying bound antibody. Critically, while Scheiflinger relates to the "determination of **anti-vWF-cp antibody** in a sample" (*see* p. 1, para. [0009]), Applicants' invention relates to a method of determining the severity of thrombophilia, comprising measuring **a von Willebrand factor-cleaving protease** from a sample of bodily fluid. Moreover, Scheiflinger certainly cannot be considered to disclose a method of determining the severity of thrombophilia in patients suffering certain ailments by correlating the amount of vWF-cp to that of a normal person, with a lower level indicating an increased severity of thrombophilia. Scheiflinger does not contemplate these claim elements, and even teaches away from them. Indeed, on page 5, paragraph [0056], Scheiflinger states that patients #1 (suffering from acute TTP) and #2 (in remission after TTP) had the same levels of vWF-cp *as normal human plasma*. Since the TTP patients had the same vWF-cp levels as normal human plasma, a skilled artisan certainly would not correlate the amount of vWF-cp in patients suffering from different ailments (*i.e.* pulmonary embolism, cerebral infarction, veno-occlusive disease, and/or deep vein thrombosis, as Applicants claim) to that of a normal person, with a lower level indicating an increased severity of thrombophilia. Rather, based on Scheiflinger, a skilled artisan would believe that both sick and normal humans would have the same levels.

As is clearly established above, Scheiflinger's emphasis is on measuring the amount of anti-vWF-cp *antibodies* in a sample, and not on detecting vWF-cp itself. Accordingly, Applicants respectfully urge that claim 1 is not anticipated. Claim 6 is directed to a kit for detecting and analyzing the degree of thrombophilia in a patient suffering from pulmonary

embolism, cerebral infarction, veno-occlusive disease, and/or deep vein thrombosis, and is believed allowable for the same reasons as claim 1. Finally, claim 7 encompasses a method of determining the severity of thrombophilia in a patient suffering from pulmonary embolism, cerebral infarction, veno-occlusive disease, and/or deep vein thrombosis, and is also believed allowable for the reasons articulated above. The remaining rejected claims depend from claims 1 and 7 and are likewise believed allowable as depending from an allowable claim.

B. Rejection of Claims 1, 3, and 5-10 as Inherently Anticipated by Konetschny in light of Scheiflinger

The Office Action rejects claims 1, 3, and 7-10 under 35 U.S.C. §102(a) as being inherently anticipated by Konetschny *et al.* (Development of a Highly Sensitive and Specific Enzyme-linked Immunosorbent Assay for the Detection of ADAMTS-13 in Human Plasma, Blood 102 (11) Abstract #4062 (November 16, 2003) (hereinafter referred to as "Konetschny") in light of Scheiflinger. Konetschny appears to be largely cumulative to Scheiflinger, who is actually a co-author on the Konetschny reference. Applicants respectfully urge that Konetschny does not anticipate Applicants' claims because the reference does not teach all of Applicants' claim limitations. For example, as discussed below, Konetschny does not teach, *inter alia,* (1) a method of determining the severity of thrombophilia comprising measuring a vWF-cp from a sample of a patient suffering from pulmonary embolism, cerebral infarction, veno-occlusive disease, and/or deep vein thrombosis, as required by Applicants' claims; or (2) comparing vWF-cp from a patient suffering from one of the enumerated diseases with that of a normal person, with a lower level present in the sample being indicative of an increased severity of thrombophilia.

Konetschny does not teach a method of determining the severity of thrombophilia comprising measuring a vWF-cp from a sample of a patient suffering from pulmonary embolism, cerebral infarction, veno-occlusive disease, and/or deep vein thrombosis, as required by Applicants' claims. The Office Action arrives at this recitation by stating that "Scheiflinger et al… teach that thrombosis as taught in the method of Konetschny et al. is manifested in patients suffering from **cancer-associated TM** in [0034]." Office Action, p. 7. Applicants respectfully submit that this reiterated rejection is moot in view of Applicants' December 3, 2010 Response,

which amended the independent claims to recite that the patient is suffering from pulmonary embolism, cerebral infarction, veno-occlusive disease, and/or deep vein thrombosis. As articulated in their last response, cancer-associated TM indications have been removed from Applicants' claims, and accordingly, the rejection is believed to be moot.

Furthermore, similar to Scheiflinger, Konetschny does not teach or even contemplate comparing vWF-cp from a patient suffering from one of the claimed enumerated diseases with that of a normal person, with a lower level present in the sample being indicative of an increased severity of thrombophilia. In fact, as discussed above, Scheiflinger (the applicant of which is a co-author of Konetschny), states that patients #1 (suffering from acute TTP) and #2 (in remission after TTP) had the same levels of vWF-cp *as normal human plasma*. *See Scheiflinger,* p. 5, para. [0056]. In view of the teaching that the TTP patients had the same vWF-cp levels as normal human plasma, a skilled artisan certainly would not correlate the amount of vWF-cp in patients suffering from different ailments (*i.e.* pulmonary embolism, cerebral infarction, veno-occlusive disease, and/or deep vein thrombosis, as Applicants claim) to that of a normal person, with a lower level indicating an increased severity of thrombophilia. Rather, based on Scheiflinger, a skilled artisan would believe that both sick and normal humans would have the same levels. Accordingly, Applicants respectfully urge that the claims are patentable, and are not anticipated by the cited art.

Finally, Applicants respectfully point out that, as explained in the MPEP, "'[a]n invitation to investigate is not an inherent disclosure' where a prior art reference 'discloses no more than a broad genus of potential applications of its discoveries.'" (MPEP § 2112(IV) (citing *Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings*, 370 F.3d 1354, 1367 (Fed. Cir. 2004) (explaining that "[a] prior art reference that discloses a genus still does not inherently disclose all species within that broad category" but must be examined to see if a disclosure of the claimed species has been made or whether the prior art reference merely invites further experimentation to find the species.) According to the MPEP, **"[i]n relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art**." (MPEP § 2112(IV) (citing *Ex parte Levy,* 17 USPQ2d 1461, 1464 (BPAI 1990) (emphasis in original))). Applicants urge that the above-discussed

teachings of Scheiflinger (TTP patients having the same level of vWF-cp as a normal human) prove that Applicant's invention cannot be considered to necessarily flow from the teachings of the cited art.

V. CONCLUSION

In view of the foregoing, reconsideration and withdrawal of the rejections are respectfully requested.

No fees are believed due. However, the Commissioner is hereby authorized to charge any fees that may be required, or credit any overpayment, to Deposit Account No. 08-1935, Reference No. 2352.014.

There being no other outstanding issues, it is believed that the application is in condition for allowance, and such action is respectfully requested.

If a telephone conference would be of assistance in advancing the prosecution of the subject application, Applicants' undersigned attorney invites the Examiner to telephone her at the number provided.

Respectfully submitted,

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